Remarks

As the amendment filed on July 3, 2002, was not entered, Applicants have reiterated the amendments. Upon entry of the foregoing amendment, claims 157, 159-160, 162-163, 165-166, 168-176, 179-180, 182-183, 185-186, 188-189 and 191-228, 230 and 232-287 will be pending in the application. Claims 158, 161, 164, 167, 174, 177, 178, 181, 184, 187, 190, 229, 231, 248, 251 and 288-294 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the canceled claims in one or more continuing applications.

Claims 157, 159, 162, 165, 168, 173, 176, 180, 182, 185, 188, 191, 196, 197, 199, 200, 207, 208, 210, 211, 230, 232, 233, 234, 235, 236, 237, 238, 239, 240, 242, 247, 250, 257, 258, 260, 261, 264, 273, 274, 276 and 277 have been amended as discussed during the recent Examiner interview. Support for amended claim 157 (and dependent claims) can be found in original claims 1 and 11, part (a). As the Examiner requested, Applicants have inserted a paragraph containing the subject matter of original claims 1 and 11, part (a), into the specification at page 6, after line 18. Support for amended claim 180 (and dependent claims) can be found, *inter alia*, at pages 11-14 of the specification.

Claims 159, 162, 165, 168, 182, 185, 188 and 191 were amended to place the claims into proper dependent format. The remaining claims were amended as discussed during the Examiner interview. This amendment introduces no new matter and entry thereof is respectfully requested. Applicants reserve the right to pursue the subject matter of the unamended claims in one or more continuing applications.

Based on the above amendments and the following remarks, Applicants respectfully

request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Examiner Interview

Applicants thank Examiner Priebe for the courteous and helpful telephonic interview extended to Applicants' undersigned representative on September 12, 2002.

Specification

The Examiner objected to the specification as allegedly failing to provide proper antecedent basis for the claimed subject matter. (Paper No. 34, at page 2.) According to the Examiner, "[t]here is no antecedent basis in the specification as originally filed for claims 159, 162, 165, 168, 182, 185, 188, 191, 229, and 231" and "new claims broadly reciting 'at least 90% identity' in the absence of a recited 'essential property' are not supported in the original disclosure, and accordingly are rejected under 35 USC 112, first paragraph for the introduction of new matter." *Id.* at pages 2-3.

Without admitting to the Examiner's allegation, and solely in the interest of facilitating prosecution, Applicants have amended the claims to recite 95% identity. As the Examiner acknowledged, support for this amendment can be found in original claims 1 and 11, part (a), the subject matter of which was inserted into the specification at page 6, after line 18. In the Advisory Action, the Examiner indicated that the amendment to the specification would overcome the objection to the specification. (Paper No. 41, at page 3.) Accordingly, this objection should be moot.

Rejections under 35 U.S.C. § 112

Written description

Claims 157-158, 161, 164, 167, 170-181, 184, 187, 190, 193-202, 207-208, 210-211, 236-237, 239-240, 247-248, 250-251, 257-258, 260-261 and 264-294 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. (Paper No. 34, at page 3.) The Examiner did not enter the amendment filed on July 3, 2002, but indicated that the claims as amended would be allowable. (Paper No. 41, at page 2.)

Solely in the interest of facilitating prosecution, Applicants have amended the claims to recite 95% identity. As the Examiner acknowledged, support for this amendment can be found in original claims 1 and 11, part (a), the subject matter of which was inserted into the specification at page 6, after line 18. Accordingly, withdrawal of this rejection is respectfully requested.

Regarding claims 176, 196, 199, 207, 210, 236, 239, 247, 250, 260, 273 and 276, the Examiner alleged that "[w]hile the specification fully supports the linkage between heterologous sequences in general to the first nucleic acid, the same cannot be said for an 'operable linkage'." (Paper No. 34, at page 5.) The Examiner maintained the rejection in the Advisory Action. (Paper No. 41, at page 2.)

Without admitting to the Examiner's allegation, and solely in the interest of facilitating prosecution, Applicants have amended the claims to recite that the "polynucleotide comprises a nucleotide sequence heterologous to said first nucleic acid."

During the Examiner interview, the Examiner indicated that such an amendment would overcome the rejection. Accordingly, withdrawal of this rejection is respectfully requested.

In the Advisory Action and during the Examiner interview, the Examiner indicated that claims 197, 200, 208, 211, 237, 240, 258, 261, 274 and 277 would be allowable if the claims were amended to indicate that "the heterologous sequence 'selected' is operably associated with the 'nucleic acid' . . . . (Paper No. 41, at page 2.)

Solely in the interest of facilitating prosecution, Applicants have amended the claims accordingly. Thus, withdrawal of this rejection is respectfully requested.

Applicants have canceled claims 288-294 without prejudice or disclaimer. Thus, the rejection of claims 288-294 has been rendered moot.

Enablement

The Examiner maintained the rejection of claims 180-182, 184-185, 187-188, 190-191, 193-202, 229, 231 and 233-242 under 35 U.S.C. § 112, first paragraph, for lack of enablement. (Paper No. 37, at page 3 and Paper No. 41, at page 3.)

The test for enablement is whether the disclosure when filed contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. M.P.E.P. § 2164.01 at 2100-174 (August 2001). The standard applied is whether the experimentation needed to practice the invention is undue or unreasonable. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

Without admitting to the Examiner's allegations, and solely in the interest of facilitating prosecution, Applicants have amended the claims. The claims as amended recite

that the amino acid sequence is at least 99% identical to the recited reference amino acid sequences, and regulates PSA gene expression. An amino acid sequence that is at least 99% identical to amino acids 1 to 335 of SEQ ID NO:2 would differ by 3 amino acids or less. As was discussed during the Examiner interview, it was routine in the art to make at least 5 amino acid changes using methods such as site-directed mutagenesis.

For example, Loeb *et al.*, *Nature 340*:397-400 (1989) (Attachment A) reported that each amino acid of the HIV-1 protease was individually mutated using a mutagenesis procedure capable of introducing and identifying missense mutations in each residue of a protein. The mutagenesis procedure allowed Loeb *et al.* to identify functionally important regions within the protein. Inouye *et al.*, *Biochem. Biophys. Res. Comm. 179*:352-358 (1991) (Attachment B) reported that one or both of the two potential Asn-linked glycosylation sites of human follistatin were mutated using site-directed mutagenesis. Gloss *et al.*, *Biochem. 31*:32-39 (1992) (Attachment C) reported that the five cysteines of *E. coli* aspartate aminotransferase were converted either one at a time, in triplet combinations, or all five at once, to alanine by site-directed mutagenesis. Thus, as of the filing date of the captioned application, it was a matter of routine experimentation to make at least 5 amino acid changes simultaneously. Such experimentation is neither undue nor unreasonable.

In addition, pages 16 and 17 of the specification provide guidance on how to make phenotypically silent substitutions, as well as conservative substitutions. The specification also provides, *inter alia*, predicted antigenic regions that comprise epitope-bearing portions of the PDEF protein (*see* page 25). One of ordinary skill in the art looking at the PDEF sequence would know which allelic or other variants that differ from SEQ ID NO:2 by 1-3

amino acid residues would, *inter alia*, be capable of raising antibodies to the native PDEF protein, and could routinely make and use the polypeptides to raise antibodies.

Since the disclosed or otherwise known methods of making and screening the claimed polypeptides may be used to determine, without undue experimentation, whether a given polypeptide encompassed by the claims can be used, *inter alia*, to make antibodies, the enablement requirement is fully satisfied. *In re Wands*, 858 F.2d at 738, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989). Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

Allowable Subject Matter

The indication that claims 203-206, 209, 212-228, 243-246, 249, 252-256, 259 and 280-287 are allowed is noted and appreciated by Applicants. (Paper No. 41.) The Examiner further indicated that claims 159-160, 162-163, 165-166, 168-169, 183, 186, 189, 192, 230 and 232 were objected to but would be allowable if rewritten in independent form, and that claims 157, 159-160, 162-163, 165-166, 168-173, 175-176, 179, 207-208, 210-211, 230, 232, 247, 250, 257-258, 260-261, 264-274, 275-278 would be allowable if amended as discussed. (*Id.* at page 2.)

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be

withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

In the Specification:

A new paragraph at page 6, after line 18, was inserted.

In the Claims:

Claims 158, 161, 164, 167, 174, 177, 178, 181, 184, 187, 190, 229, 231, 248, 251 and 288-294 were canceled without prejudice or disclaimer.

The following claims 157, 159, 162, 165, 168, 173, 176, 180, 182, 185, 188, 191, 196, 197, 199, 200, 207, 208, 210, 211, 230, 232, 233, 234, 235, 236, 237, 238, 239, 240, 242, 247, 250, 257, 258, 260, 261, 264, 273, 274, 276 and 277 were substituted for pending claims 157, 159, 162, 165, 168, 173, 176, 180, 182, 185, 188, 191, 196, 197, 199, 200, 207, 208, 210, 211, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 242, 247, 250, 257, 258, 260, 261, 264, 273, 274, 276 and 277:

157. (Once amended) An isolated polynucleotide comprising a first nucleic acid at least [90%] 95% identical to a reference nucleic acid selected from the group consisting of:

(a) a nucleic acid consisting of nucleotides 839 to 1048 of SEQ ID NO:1;

(b) a nucleic acid consisting of nucleotides 419 to 1420 of SEQ ID NO:1;

(c) a nucleic acid consisting of nucleotides 416 to 1420 of SEQ ID NO:1; and

(d) a nucleic acid consisting of the nucleotides encoding the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

159. (Once amended) The isolated polynucleotide of claim [158] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of nucleotides 839 to 1048 of SEQ ID NO:1.

162. (Once amended) The isolated polynucleotide of claim [161] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of nucleotides 419 to 1420 of SEQ ID NO:1.

165. (Once amended) The isolated polynucleotide of claim [164] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of nucleotides 416 to 1420 of SEQ ID NO:1.

168. (Once amended) The isolated polynucleotide of claim [167] 157, wherein said first nucleic acid is at least 95% identical to a reference nucleic acid consisting of the nucleotides encoding the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

173. (Once amended) The vector of claim 172, wherein said [first nucleic acid is

operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

176. (Once amended) The host cell of claim 175, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

180. (Once amended) An isolated polynucleotide comprising a nucleic acid encoding a first amino acid sequence at least [90%] 99% identical to a reference amino acid sequence selected from the group consisting of:

(a) amino acids 142 to 211 of SEQ ID NO:2;

(b) amino acids 2 to 335 of SEQ ID NO:2;

(c) amino acids 1 to 335 of SEQ ID NO:2; and

(d) the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072;

wherein said first amino acid sequence regulates Prostate-Specific Antigen (PSA) gene expression.

182. (Once amended) The isolated polynucleotide of claim [181] 180, wherein said first amino acid sequence is at least [95%] 99% identical to amino acids 142 to 211 of SEQ ID NO:2.

185. (Once amended) The isolated polynucleotide of claim [184] 180, wherein said first amino acid sequence is at least [95%] 99% identical to amino acids 2 to 335 of SEQ ID NO:2.

188. (Once amended) The isolated polynucleotide of claim [187] 180, wherein said first amino acid sequence is at least [95%] 99% identical to amino acids 1 to 335 of SEQ ID NO:2.

191. (Once amended) The isolated polynucleotide of claim [190] 180, wherein said first amino acid sequence is at least [95%] 99% identical to the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 203072.

196. (Once amended) The vector of claim 195, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

197. (Once amended) The vector of claim 196, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

199. (Once amended) The host cell of claim 198, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

200. (Once amended) The host cell of claim 199, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

207. (Once amended) The vector of claim 206, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

208. (Once amended) The vector of claim 207, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

210. (Once amended) The host cell of claim 209, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

211. (Once amended) The host cell of claim 210, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

230. (Once amended) [The] An isolated polynucleotide [of claim 229,] comprising a nucleic acid encoding at least 100 contiguous amino acids of SEQ ID NO:2.

232. (Once amended) The isolated polynucleotide of claim [231] 230, comprising a nucleic acid encoding at least 150 contiguous amino acids of SEQ ID NO:2.

233. (Once amended) The isolated polynucleotide of claim [229] 230, further comprising a nucleotide sequence heterologous to said nucleic acid.

234. (Once amended) A method of producing a vector comprising inserting the isolated polynucleotide of claim [229] 230 into a vector.

235. (Once amended) A vector comprising the isolated polynucleotide of claim [229] 230.

236. (Once amended) The vector of claim 235, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

237. (Once amended) The vector of claim 236, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

238. (Once amended) A host cell comprising the isolated polynucleotide of claim [229] 230.

239. (Once amended) The host cell of claim 238, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

240. (Once amended) The host cell of claim 239, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

242. (Once amended) A composition comprising the isolated polynucleotide of claim [229] 230.

247. (Once amended) The vector of claim 246, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

250. (Once amended) The host cell of claim 249, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said first nucleic acid.

257. (Once amended) The vector of claim 256, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

258. (Once amended) The vector of claim 257, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

260. (Once amended) The host cell of claim 259, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

261. (Once amended) The host cell of claim 260, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

264. (Once amended) A polynucleotide comprising a nucleic acid fused in frame to a nucleotide sequence heterologous to SEQ ID NO:1, wherein said heterologous nucleotide sequence encodes a heterologous polypeptide, and wherein said nucleic acid is selected from the group consisting of:

(a) a nucleic acid encoding amino acids 279 to 287 of SEQ ID NO:2;

(b) a nucleic acid encoding amino acids 292 to 300 of SEQ ID NO:2;

(c) a nucleic acid encoding amino acids 317 to 325 of SEQ ID NO:2;

(d) a nucleic acid encoding amino acids 239 to 247 of SEQ ID NO:2;

(e) a nucleic acid encoding amino acids 272 to 280 of SEQ ID NO:2; and

(f) a nucleic acid encoding amino acids 248 to 331 of SEQ ID NO:2.

273. (Once amended) The vector of claim 272, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

274. (Once amended) The vector of claim 273, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.

276. (Once amended) The host cell of claim 275, wherein said [first nucleic acid is operably associated with] polynucleotide comprises a nucleotide sequence heterologous [sequence] to said nucleic acid.

277. (Once amended) The host cell of claim 276, wherein said heterologous sequence is operably associated with said nucleic acid and is selected from the group consisting of a promoter, a site for transcription initiation, a site for transcription termination, an enhancer, a Kozak sequence, an operator and a ribosome binding site.